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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/074,257	02/14/2002	Chih-Pin Liu	1954-313	5061

6449 7590 10/11/2005

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EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/074,257	LIU ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,10-16,23-25,32-34,53 and 54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,10-16,23-25,32-34,53 and 54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08092005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application claims the benefit of the filing date of provisional application 60/268,714.

Claims 5-9, 17-22, 26-31 and 35-52 have been canceled.

New claims 53-54 have been added.

Claims 1-4, 10-16, 23-25, 32-34 and 53-54 are currently pending.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 9, 2005 has been entered.

Election/Restrictions

2. Applicant has canceled all claims drawn to non-elected inventions previously held as withdrawn.

3. It is noted that, upon the filing of the RCE, Applicant has amended the claims to read upon GAD-specific MHC class II complexes of a murine I-Ag7 haplotype or a human HLA-DQ haplotype complexed a GAD peptide. The claimed invention is broader in scope than the recombinant construct of a GAD peptide sequence linked to an MHC class II beta chain. The claims now read upon any I-Ag7 or HLA-DQ complex comprising a GAD peptide.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-4, 13-16, 23-25, 32-34 and 53-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was

not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth the GAD peptides identified by SEQ ID NOs: 1-13 as being capable of binding to the murine I-Ag7 or human HLA-DQ haplotypes.

The claims are broadly drawn to MHC class II complexes of murine I-Ag7 or human HLA-DQ haplotypes comprising any GAD peptide that binds to the MHC class II molecule. The specification does not identify specific anchor residues required within antigenic peptide sequences that are required for MHC class II recognition of the peptides, nor does the specification identify where else in the GAD proteins the anchor residues can be found. Applicant has identified only 13 peptide sequences of 20 or fewer amino acid residues in length as epitopes for the specified MHC class II haplotypes out of a protein that is at least about 65kD in size. Accordingly, the 13 peptides identified by the specification do not represent the entire genus of potential epitopes within the sequence of GAD.

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111), clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is.claimed." (See *Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115).

With the exception of SEQ ID NOs: 1-13, the skilled artisan cannot envision GAD peptides that bind to murine I-Ag7 or human HLA-DQ haplotypes without an adequate description of required anchor residues and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of identifying the peptides. Adequate written description requires more than a mere statement that it is part of the invention and a reference to antibodies which penetrate cells (page 9, lines 14-35 of the instant specification. See *Fiers v. Revel*, ((CAFC, 1993) 25 USPQ 2d 1601) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*,((CAFC, 1991) 18 USPQ2d 1016).

Therefore, the only GAD peptides adequately described are those that comprise a sequence selected from the group consisting of SEQ ID NOs: 1-13 meet the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 1-4, 10-13, 15, 23, 24 and 32-34 are rejected under 35 U.S.C. 102(a) as being anticipated by Yu et al. (Eur. J. Immunol. [2000] 30:2497-2506; U on form PTO-892).

The claims are broadly drawn to MHC class II murine I-Ag7 or human HLA-DQ complexes comprising a peptide from GAD. Yu teaches recombinant soluble human HLA-DQ8 complexes comprising an alpha chain and a beta chain, both of which have had their transmembrane regions removed and replaced with leucine zipper sequences (page 2498, column 1 in particular) [claims 1-4, 23]. Yu further teaches that the complex bound a number of different GAD peptides, including peptides instantly disclosed as SEQ ID NOs: 1-6, 10 and 11 (Table 1 in particular) [claims 10-12]. Yu also teaches that the complexes are detected by using direct biotinylation of the peptides (page 2498, column 2 in particular) [claims 13, 15, 24, 32] and reaction of the biotinylated complex with a radiolabeled effector-avidin in the form of europium-labeled streptavidin (Table 1 and Figure 3 in particular) [claims 33-34]. The prior art teaching anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-2, 14, 16, 23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (Eur. J. Immunol. [2000] 30:2497-2506; U on form PTO-892) in view of U.S. Patent No. 6,232,445 to Rhode et al (patent date May, 15, 2001, filed October 29, 1997; of record).

Yu has been discussed supra, as being anticipatory to claims 1-2 and 23.

The reference does not teach oligohistidine tags.

The '445 patent further teaches that recombinantly produced soluble MHC molecules can be engineered to comprises a tail or "tag," such as oligohistidine (6x-His) that can be used for purification [claims 10, 14, 16 and 25] (column 27, lines 8-20 and column 54, lines 59-64).

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of Yu with the teachings of the '445 patent to create MHC class II complexes comprising GAD 65 peptide antigens and bearing an oligohistidine tag. The artisan would have been motivated to combine the teachings with a reasonable expectation of success to create to create soluble single-chain MHC class II molecules of human HLA-DQ8 molecules by combining the teachings of Yu as set forth supra and tagging the molecules by incorporating an oligohistidine tail as taught by the '445 patent distal to the leucine zipper motifs in order to simplify the purification of the recombinantly produced molecules from culture medium.

7. Claims 1, 23 and 53-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (Eur. J. Immunol. [2000] 30:2497-2506; U on form PTO-892) in view of U.S. Patent No. 5,635,363 to Altman et al (patent date June 3, 1997; A on form PTO-892).

Yu has been discussed supra, as being anticipatory to claims 1 and 23.

The reference does not teach MHC class II tetramers.

The '363 patent teaches the making of MHC class II multimers, including the making of tetramers, for example, by biotinylating the MHC class II peptides and reacting them with streptavidin, which has a valency of 4, resulting in the formation of a tetramer (column 6, lines 51-57 in particular).

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of Yu with the teachings of the '363 patent to make tetramers of MHC class II molecules. One would have been motivated to combine the teachings, with a reasonable expectation of success, by the teachings of the '363 patent that "[w]hen compared to the binding of an MHC "monomer" to a T cell, the binding complex will have greatly increased stability, usually having an increase of at least about 10-fold in t1/2, more usually an increase of about 20-fold, and may be increased as much as about 50-fold" (column 3, lines 20-32 in particular).

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
September 30, 2005

David a Saunders

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